Complete Summary

GUIDELINE TITLE

Methadone and buprenorphine for the management of opioid dependence.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Methadone and buprenorphine for the management of opioid dependence. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 37 p. (Technology appraisal guidance; no. 114).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Opioid dependence

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Pharmacology
Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Substance Use Disorders Treatment Providers

GUIDELINE OBJECTIVE(S)

- To assess the clinical and cost effectiveness of buprenorphine maintenance therapy (BMT) and methadone maintenance therapy (MMT) for the management of opioid dependent individuals from the perspective of the National Health Service and Personal Social Services

  Three specific questions were addressed:

  - Is MMT effective and cost effective compared to no drug therapy?
  - Is BMT effective and cost effective compared to no drug therapy?
  - Is MMT or BMT more effective and cost effective?
- To explore the potential variation in effectiveness of BMT and MMT across drug dose, patient subgroups and treatment settings; assess the cost-effectiveness of BMT and MMT from a wider societal perspective; and compare the effectiveness of BMT compared to buprenorphine detoxification (BDT) and MMT compared to methadone detoxification (MDT)

TARGET POPULATION

Opioid dependent adults (18 years and over)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Methadone
2. Buprenorphine

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
  - Changes in illicit drug use (frequency of use, type of use, dosage)
  - Proportion of patients remaining illicit-drug free
  - Retention in treatment
  - Compliance with recommended dose
  - Quality of life
  - Side effects and adverse effects of treatment drugs
  - Illicit-drug related morbidity (e.g., blood borne virus infection)
  - Mortality

    - Non-health outcomes of criminal activity and employment
- Cost-effectiveness of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the West Midlands Health Technology Assessment Collaboration (see the "Availability of Companion Documents" field.)

Clinical Effectiveness

Identification of Studies

Review of Systematic Reviews

Searches for existing systematic reviews (that included randomised controlled trials [RCTs] or non-RCTs) were undertaken using the Aggressive Research Intelligence Facility (ARIF) search protocol which includes sources such as Cochrane Library, internet sites of health technology assessment organisations, and MEDLINE (see Appendix 1 in the Assessment Report [see "Availability of Companion Documents" field]). In addition the Cochrane Drugs and Alcohol Group were contacted to seek any recent updates of current Cochrane reviews. The searches were not restricted by date or language.

Review of Recent Randomised Controlled Trials

The following sources were searched for RCTs:

- Bibliographic databases: Cochrane Library (CENTRAL)(Wiley internet interface) 2005 Issue 3, MEDLINE (Ovid) 2001–Aug 2005, MEDLINE In-Process & Other Non-Indexed Citations (Ovid) 12 Aug 2005, EMBASE (Ovid) 2001–Aug 2005, PsycINFO (Ovid) 2001–Aug 2005, International Bibliography of the Social Sciences(BIDS) 2001–Aug 2005, Sociological Abstracts (CSA Illumina) 2001–2005. Searches were based on text words and index terms, where available, which encompassed methadone, buprenorphine; opioid misuse, dependence, and withdrawal. No language restrictions were applied. (see Appendix 1 in the Assessment Report for full search strategies [see "Availability of Companion Documents" field.])

- Citations of relevant studies
- Further information was sought from contact with author reports where necessary
- Research registers of ongoing studies were searched as follows: National Research Register 2005 Issue 3, Current Controlled Trials and ClinicalTrials.gov.
- Invited industry submissions to NICE for this appraisal

Inclusion and Exclusion Criteria

Review of Systematic Reviews

A systematic review was defined for the purposes of this report as a review that stated that at least one substantial database (e.g., EMBASE) had been scrutinised in conjunction with appropriate search terms. Meta-analyses were also included if they satisfied this criterion. In addition reviews were included if their inclusion criteria encompassed:

- Studies of opioid dependent individuals
- Studies (RCTs or non RCTs) of methadone and/or buprenorphine as maintenance therapy or detoxification strategies

Foreign language reviews were excluded, but those of potential relevance were identified and commented upon. Two reviewers independently undertook the selection of reviews with a third reviewer resolving any disagreement.

Review of Recent Randomised Controlled Trials

RCTs were included if they had not already been analysed and considered within included systematic reviews. Further inclusion criteria for RCTs were that they encompassed:

- A population of opioid dependent individuals
- Study of methadone and or buprenorphine as maintenance therapy or detoxification strategies

RCTs were excluded if the population was a mixture of cocaine abusers and opioid abusers, or if the population were in methadone or buprenorphine maintenance, temporarily switched prior to randomisation to an alternative, and subsequently randomly allocated back to methadone or buprenorphine maintenance (with or without supplementary pharmacotherapy or other therapy). Two reviewers undertook selection of RCTs and a third reviewer resolved disagreement.

Cost-Effectiveness

Search Strategy

A comprehensive search for literature on the cost and cost effectiveness of methadone and buprenorphine as substitute opiates for opioid dependent drug misusers was conducted. The searches identified existing economic models and

information on costs, cost effectiveness, and quality of life from the following sources:

- Bibliographic databases: MEDLINE (Ovid) 1966–week 1 2005, EMBASE (Ovid) 1980–Aug 2005, Cochrane Library (NHS EED and DARE) (Wiley internet interface) 2005 Issue 3, HEED database Aug 2005.
- Industry submissions.
- Internet sites of national economic units.

Full details of search strategies are contained in Appendix 1 of the Assessment Report (see "Availability of Companion Documents" field).

Inclusion and Exclusion Criteria

The following inclusion criteria were used:

Study Design: Cost-consequence analysis, cost-benefit analysis, cost-effectiveness analysis, cost-utility analysis, cost studies (UK only), and quality of life studies.

Population: People who are dependent on opioids

Interventions: Buprenorphine or methadone employed in maintenance therapy irrespective of dose. The following operational definition was employed: any trial that calls itself "maintenance" or any trial that does not include a reducing or cessation of methadone/buprenorphine dose as part of its intervention.

Comparator: Any comparator regime used in maintenance therapy (including no therapy or placebo) or the intervention drug used in withdrawal/detoxification therapy.

Outcome: Quality of life estimates, cost estimates, cost-effectiveness

Study Selection

An experienced health economist applied the inclusion and exclusion criteria – checked by a second health economist.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

31 systematic reviews were included in this report. In addition, 27 RCTs were included.

Cost-Effectiveness

Previous Economic Evaluations

Eleven published economic evaluations met the inclusion criteria.

Industry Economic Evidence

Two industry submissions were received – Schering Plough for buprenorphine and Cardinal Health for methadone. Only Schering-Plough submitted cost effectiveness evidence.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the West Midlands Health Technology Assessment Collaboration (see the "Companion Documents" field.)

Clinical Effectiveness

Critical Appraisal Strategy

Review of Systematic Reviews

The methodological quality and quality of reporting of the included systematic reviews and meta-analyses was assessed using the validated Overview Quality Assessment Questionnaire (OQAC) instrument developed by Oxman et al 1991*.

Review of Recent Randomised Controlled Trials (RCTs)

The methodological quality of included RCTs was assessed on the basis of randomisation, adequate concealment of randomisation, level of blinding, use of intention-to-treat-analysis, and description of loss to follow up. An overall quality score (Jadad) was assigned to each RCT using a modified Jadad instrument (see Appendix 5 in the Assessment Report [see "Availability of Companion Documents" field] for details on quality assessment instruments).

* Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. *J Clin Epidemiol* 1991; **44**(11):1271-1278.

Data Extraction

One reviewer extracted data from systematic reviews and RCTs into pre-designed data forms. Extracted data was checked by at least one other reviewer and disagreement resolved by discussion. Data from studies with multiple publications were reported as a single study, but the source of publications noted.

For both included systematic reviews and RCTs, the following outcomes were sought:

- Drug use, i.e., changes in illicit drug use; concordance with, and retention in treatment
- Health of drug user, i.e., drug-related mortality; drug-related morbidity (e.g., blood-borne virus infection rates); health-related quality of life; use of health care system; major adverse effects of treatment (i.e., drug interactions, liver disease, cardiac abnormality, exacerbation of comorbidity)
- Social effects, i.e., effects on employment; effects on family
- Effects on criminal justice system i.e., rates of crime; recidivism

Economic Analyses

Data Extraction and Quality Assessment Strategy

Data were extracted by one reviewer using a pre-designed data extraction form and were independently check by a second reviewer. Data on the following were sought:

- Study characteristics, such as study question, form of economic analysis, population, interventions, comparators, perspective, time horizon, and modelling used.
- Clinical effectiveness and cost parameters, such as effectiveness data, health state valuations (utilities), resource use data, unit cost data, price year, discounting, and key assumptions.
- Results and sensitivity analyses.

These characteristics and the main results of included economic evaluations are summarized in Tables 8 to 11 of the Technology Assessment Report (see "Availability of Companion Documents" field). The quality of included studies and industry submissions was assessed using an adapted version of the Drummond and Jefferson BMJ criteria for economic evaluations was used to assess non-model studies and the Phillips (2004) Consensus on Health Economic Criteria quality criteria was used to assess economic model reports. The use of the predetermined quality criteria was agreed at the outset of the review. In the first instance the quality of economic aspects of the studies was assessed. Papers failing more than two quality criteria were excluded. Papers failing two items were reviewed to identify key messages contained in the papers and marked with a query. Papers that failed just one or none of the items were reviewed in full and marked with a pass.

The final data on incremental cost effectiveness ratios (ICERs) extracted from the relevant papers were converted from their respective currencies to sterling using

purchasing power parities from the Organization for Economic Cooperation and development. Once converted to sterling the cost data were inflated to 2004 prices using the National Health Services (NHS) Executive Hospital and Community Health Services Pay and Prices inflation index.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Eight studies assessed the cost effectiveness of methadone maintenance therapy (MMT), one assessed the cost effectiveness of buprenorphine maintenance therapy (BMT), and two compared the cost effectiveness of BMT directly with that of MMT. The studies reported results using a range of outcome measures. The Assessment Group reported that direct comparison of the incremental cost-effectiveness rations (ICERS) between the studies was not possible because of differences in the approaches to modelling, time horizons, comparators and perspective, country of origin, source of preference weights, and effectiveness data used.

Although most of the included papers were considered to be of high quality, none used all of the appropriate parameters, effectiveness data, perspectives, and comparators required to make their results generalisable to the National Health Service (NHS) and personal social services (PSS).

Manufacturers' Models

No economic evaluations were submitted by the manufacturers of methadone oral solution.

The manufacturer of buprenorphine (Schering-Plough) submitted a cost-effectiveness analysis of BMT compared with MMT for opioid-dependent people over a 1-year time horizon. Cost effectiveness was assessed as the incremental cost per quality-adjusted life year (QALY) using a decision-tree-based model. Costs were calculated from an NHS and PSS perspective. Both simple one-way and probabilistic sensitivity analyses were undertaken.

The model was designed to estimate the cost effectiveness of BMT in three scenarios: BMT compared with no treatment for the 20% of opioid-dependent people seeking maintenance treatment who are unable to take methadone for "clinical reasons" (as stated by the manufacturer); BMT compared with MMT for the remaining 80% of opioid-dependent people; and maintenance therapy

(methadone and buprenorphine) compared with drug-free treatment for all opioid-dependent people.

Assessment Group's Model

The Assessment Group developed a decision tree with Monte Carlo simulation to assess the cost effectiveness of BMT and MMT compared with drug-free therapy, and of BMT compared with MMT. The model estimated costs and outcomes from an NHS and PSS perspective for a 12-month period for the three strategies. Maintenance therapy was assumed to be a flexible dosing regimen, and the mean daily dose was assumed to be constant from week 13 onwards. The average cost of dispensing drugs was based on assumptions of supervised self-administration 6 days a week for the first 3 months, then unsupervised self-administration 6 days a week from 3 to 6 months, and unsupervised self-administration three times a week from 6 to 12 months. In addition to drug costs, estimates of resource use included counselling sessions, monitoring of treatment, general practitioner (GP) visits, emergency department visits, inpatient hospital stays, outpatient mental health appointments and inpatient mental health admissions.

See section 4.2 in the original guideline document for a complete summary of the evidence of cost effectiveness from the manufacturer and the economic evaluation undertaken by the Assessment Group.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- Methadone and buprenorphine (oral formulations), using flexible dosing regimens, are recommended as options for maintenance therapy in the management of opioid dependence.
- The decision about which drug to use should be made on a case-by-case basis, taking into account a number of factors, including the person's history

of opioid dependence, their commitment to a particular long-term management strategy, and an estimate of the risks and benefits of each treatment made by the responsible clinician in consultation with the person. If both drugs are equally suitable, methadone should be prescribed as the first choice.

- Methadone and buprenorphine should be administered daily, under supervision, for a least the first 3 months. Supervision should be relaxed only when the patient's compliance is assured. Both drugs should be given as part of a programme of supportive care.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of methadone and buprenorphine for the management of opioid dependence

POTENTIAL HARMS

Methadone

Initiation of treatment with methadone presents a potential risk of respiratory depression and should be undertaken with care. Interactions between methadone and other respiratory depressants such as alcohol, benzodiazepines and the newer non-benzodiazepine hypnotics (Z-drugs), other sedatives, or tricyclic antidepressants may also induce serious respiratory depression. There is a risk of death early in methadone treatment as a result of excessive initial doses, failing to recognise cumulative effects, giving methadone to people with impaired liver function (due to chronic hepatitis), or failing to inform patients of the dangers of overdose if they are using other drugs at the same time. The relatively slow onset of action and long half-life mean that methadone overdose and toxic effects may become life threatening several hours after a dose is taken. During the initiation phase, the methadone dose should be adjusted carefully in order to eliminate drug craving and prevent withdrawal while avoiding the risk of intoxication or overdose.

Buprenorphine

Buprenorphine has a relatively good safety profile. Even higher than normal therapeutic doses rarely result in clinically significant respiratory depression

because of its partial agonist activity at the opioid receptor involved (mu). The safety of buprenorphine mixed with high doses of other sedative drugs such as alcohol or benzodiazepines remains unclear. Starting buprenorphine treatment in opioid-dependent people may precipitate symptoms of withdrawal because buprenorphine displaces any residual illicit opioid agonists from receptors and because its partial agonist activity reduces the stimulation of receptors. In addition, whereas methadone is an agonist, buprenorphine is an antagonist at the receptor subtype involved in mood (kappa), which may mean that it produces less dysphoria. Buprenorphine has abuse potential, as tablets can be crushed and then injected.

For full details of side effects and contraindications, see the Summary Product Characteristics (SPC) available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation

- The Healthcare Commission assesses the performance of National Health Services (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (www.nice.org.uk/TA114) (see also the "Availability of Companion Documents" Field).
    - Local costing template incorporating a costing report to estimate the savings and costs associated with implementation.
    - Audit criteria to monitor local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Methadone and buprenorphine for the management of opioid dependence. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 37 p. (Technology appraisal guidance; no. 114).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jan

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Methadone and buprenorphine for the management of opioid dependence. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 2 p. (Technology appraisal 114). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Methadone and buprenorphine for the management of opioid dependence. Costing template and costing report. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. Various p. (Technology appraisal 114). Available from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Methadone and buprenorphine for the management of opioid dependence. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 12 p. (Technology appraisal 114). Available from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. Assessment report. West Midlands Health Technology Assessment Collaboration, University of Birmingham. 2005 Jan. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1174. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Methadone and buprenorphine for managing opioid dependence. Understanding NICE guidance – Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 4 p. (Technology appraisal 114).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1175. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on June 25, 2007.

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